

Amendments to the specification:

Please replace paragraph 12 with the following paragraph:

61 [0012] The interference of exogenous hemoglobin, or oxygen-carrying blood substitutes, in a blood sample with the measurement of mean cell hemoglobin content (~~MHC~~ MCH) value, mean cell hemoglobin concentration (MCHC) value, as well as with a number of blood chemistry assays can be corrected by a manual (unautomated) multistep process which requires centrifuging an anticoagulated whole blood sample and obtaining a measurement of the plasma hemoglobin. The plasma hemoglobin (or serum hemoglobin) measurement is then used to recalculate manually the erroneous results. For example, for hematology:

Whole Blood Concentration of Red Blood Cell Derived Hemoglobin, or Cell Derived Hemoglobin, (RBC HGB or Cell HGB), [units: gm/dL] = Total HGB – Plasma HGB [units: gm/dl]

MCH, (corrected), [units: picograms/cell] =
RBC HGB / RBC count [count units: cells/mm³] (x 10)

MCHC [units: gm/dL]= RBC HGB / Hematocrit (HCT) [%] (x 100);

and for chemistry:

Corrected Result = Reported Result – (Correction Factor x Serum Hemoglobin or Plasma Hemoglobin [units: (gm/dL)]).

Please replace paragraph 13 with the following paragraph:

[0013] Correction factors are routinely and empirically determined by individual clinical laboratories for various blood parameters. In the above equations and in equations in which these parameters are specified hereinbelow, the units for whole blood concentration of Red Blood Cell Derived Hemoglobin (RBC HGB), (also called Cell Derived Hemoglobin), are

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gm/dL; the units for Plasma HGB are gm/L; the units for MCH are picograms/cell; the units for RBC concentration, or cell count, are cells/mm³; the units for MCHC are gm/dL; and the unit for Hematocrit (HCT) is %.

Please replace paragraph 16 with the following paragraph:

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[0016] It is an object of the present invention to provide an automated method of overcoming the problem of interference during the automated analysis of whole blood, plasma and serum samples. The present invention preferably corrects for interference caused by cell free hemoglobin derivative compounds, which have a color to them and which therefore interfere with certain clinical tests and result parameters. The present invention provides an automated method to correct clinical chemistry results and hematology blood parameter results and values, e.g., mean cell hemoglobin content (MCH) and mean cell hemoglobin concentration (MCHC), to account for interference error. In accordance with the present invention, automated, accurate results, free from interference error, are provided in the clinical testing and analysis of blood, plasma and serum samples collected from patients who have received a blood substitute.

Please replace paragraph 18 with the following paragraph:

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[0018] The present invention provides an automated method and system to account for and correct for interference ~~to~~ and allow accurate determination of hematology and clinical chemistry parameters and values. Such interference is caused by the presence of exogenous blood substitutes, e.g. cell-free hemoglobin derivatives and oxygen-carrying blood products, in blood, plasma and serum samples analyzed by automated methods and hematology systems which detect and quantify different types of hemoglobin in whole blood samples, as well as in plasma and serum samples.

Please replace paragraph 19 with the following paragraph:

[0019] Cell-free hemoglobin derivatives typically have a red color and interfere with certain clinical tests. (Z. Ma et al., 1997, *Clin. Chem.*, 43:1732-1737). These compounds may interfere with accurate reporting of the cellular properties and blood and clinical parameters, for example,

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mean cell hemoglobin content (MCH) and Mean Cellular Hemoglobin Concentration (MCHC). Thus, interference error is associated with the presence of cell-free hemoglobin derivatives, which carry oxygen and have a red color, in the performance of whole blood cell assays using automated hematology analyzers.

Please replace paragraph 24 with the following paragraph:

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[0024] In view of this, interference correction should be applied for each sample containing an exogenous blood substitute only for those clinical methods which have interference from heme-color alone. The present automated correction method advantageously and specifically allows such correction to those samples requiring it by using the plasma hemoglobin concentration value (i.e., HGB Delta, as described below) automatically generated by the automated analyzer, such as ADVIA 120®, and an appropriate correction algorithm to attain the correct value for the desired blood parameter.

Please replace paragraph 26 with the following paragraph:

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[0026] In a preferred embodiment, automated hematology analyzers produced by and commercially available from Bayer Corporation, the assignee hereof, have been found to be able to directly determine and measure the concentration of exogenous, i.e., extracellular, hemoglobin in a sample. Suitable instruments for carrying out the analyses of the present invention possess two analytic channels which measure the whole blood concentration of hemoglobin in a blood sample. Specifically, and by way of example, the Bayer H*™ series of hematology analyzer instruments and the Bayer ADVIA® series of hematology analyzer instrument systems (e.g., ADVIA 120®) have the capability of performing quantitative analysis on the total hemoglobin content of blood and of distinguishing the hemoglobin component derived from red blood cells from that derived from the plasma.

Please replace paragraph 27 with the following paragraph:

[0027] More particularly, the Bayer hematology analyzers, are able to determine separately and independently the whole blood concentration of the cellular HGB (reported as "Calculated

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HGB”), as well as whole blood concentration of total hemoglobin (reported as “HGB”) in a whole blood sample. These hematology analyzers can simultaneously detect cellular hemoglobin and non-cellular hemoglobin, i.e., exogenously added hemoglobin, in a whole blood sample, and thus, can report the separate values of these measurements.

Please replace paragraph 32 with the following paragraph:

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[0032] As a consequence of interference, assays of patients’ blood samples for numerous blood chemistries and hematology parameters, including, but not limited to, for example, albumin, alkaline phosphatase (ALP), alanine transaminase (ALT; formerly SGPT), amylase, aspartate transaminase (AST), urea, calcium, creatinine kinase (CK), bicarbonate, creatinine, creatinine phosphokinase, muscle/brain (CKMB), total bilirubin, gamma glutamyl transferase (GGT), glucose, lactate dehydrogenase (LDH), magnesium, phosphate, lipase, mean cell hemoglobin content (~~MHC~~ MCH), mean cell hemoglobin concentration (MCHC), and preferably, albumin, ALP, amylase, calcium, bicarbonate, GGT, LDH, MCH, MCHC and total bilirubin, which are frequently affected by the presence of exogenous hemoglobin and other heme-colored oxygen-carrying blood substitute products, may not be completely accurate or correct. Accordingly, by application of the presently-described automated method, the parameter results from the automated analysis of blood samples containing blood substitutes can be corrected to accurately account for interference error, so as to achieve valid and reliable values for such blood chemistry and hematology parameter results.

Please replace paragraph 38 with the following paragraph:

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[0038] Accordingly, in one of its aspects, the automated method of the present invention corrects the parameters of mean cell hemoglobin content (MCH), (units: picograms/cell), and mean cell hemoglobin concentration (MCHC), (units: gm/L), values in a sample, particularly, a whole blood sample, containing a heme-colored interfering substance and comprises: for MCH, dividing ~~the~~ cellular hemoglobin concentration (Calculated HGB) (units: gm/dL) by the red blood cell concentration (units: cells/mm³) to obtain a first value; multiplying the first value by a first constant, ~~e.g.~~ i.e., 10, to correct for differences in units of dimensions to obtain a corrected

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MCH value; and for MCHC, dividing the cellular hemoglobin concentration (Calculated HGB) (units: gm/dL) by the hematocrit (HCT) value, (%) to obtain a second value; and multiplying the second value by a second constant, e.g.i.e., 100, to correct for differences in units of dimensions so as to obtain a corrected mean cell hemoglobin concentration (MCHC).
